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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,158	09/25/2006	Samuel J. Danishefsky	2003080-0201 (SK-1071-US1)	3195
7590 10/14/2009 Patent Department Choate, Hall & Stewart LLP Two International Place Boston, MA 02110			EXAMINER HAVLIN, ROBERT H	
			ART UNIT 1626	PAPER NUMBER
			MAIL DATE 10/14/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/551,158	Applicant(s) DANISHEFSKY ET AL.	
	Examiner ROBERT HAVLIN	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19,21-37,48-64 and 71-78 is/are pending in the application.
- 4a) Of the above claim(s) 6,14-19,21,22,25-33,36,37,48,56-64,74 and 75 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,7-13,23,24,34,35,49-55,71-73 and 76-78 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 September 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/28/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims: Claims 1-19, 21-37, 48-64, and 71-78 are currently pending.

Priority: This application is a 371 of PCT/US04/09571 (03/26/2004).

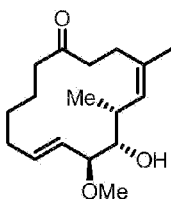
IDS: The IDS dated 9/28/05 was considered.

Election/Restrictions

1. Applicant's election with traverse of group III (claims 1-37, 48-55, and 71-78) in the reply filed on 7/8/09 is acknowledged. The traversal is on the ground(s) that a search of the subject matter of the methods of group VIII would be coextensive with group III. This is not found persuasive because consideration of the methods require an additional search which would present an undue burden. Furthermore, as detailed in the following rejection, unity of invention is lacking because the claims do not share a special technical feature over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

2. Applicant also elected the following species (stated to read on claims 1-5, 7-13, 23-24, 34-35, 49-64, 71-73, and 76-78):



As detailed in the following rejections, the generic claim encompassing the elected species was not found patentable. Therefore, the provisional election of species is given effect, the examination is restricted to the elected species only, and

claims not reading on the elected species are held withdrawn. Accordingly, claims 6, 14-19, 21-22, 25-33, 36-37, 48, 56-64, and 74-75 are hereby withdrawn.

Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection through amendment, the amended Markush-type claim will be reexamined to the extent necessary to determine patentability of the Markush-type claim. See MPEP 803.02.

Claim Rejections - 35 USC § 102

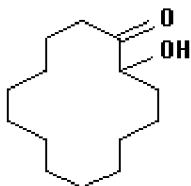
3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 2, and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al. (Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (2002), 41B(2), 423-426).

Singh et al. teaches the following compound:



Which anticipates the claims. The prior art also anticipates claim 49 (pharmaceutical composition) because giving the claim the broadest reasonable interpretation leads to the scope of water, ethanol, and xylene which is the state of prior art.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-5, 7-13, 23-24, 34-35, 49-55, 71-73, and 76-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds identified as having the asserted utility with experimental data, does not reasonably provide enablement for the asserted utility of the entirety of the claim scope. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Particularly relevant to the instant case is the issue as to whether the specification provides embodiments allowing use of the claimed invention without requiring undue experimentation by one of ordinary skill in view of the highly unpredictable nature of inhibiting enzymes or unknown pathways.

“[An inventor] must not be permitted to achieve . . . dominance by claims which are insufficiently supported and hence not in compliance with the first paragraph of 35 U.S.C. 112. That paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.” *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

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Accordingly, the critical element here how broad the claims are compared to the level of unpredictability in the art.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

Nature of Invention. The nature of the invention involves pharmaceutical compounds for inhibiting enzymes or unknown pathways.

Scope of the Invention. The scope of the invention are for a genus of compounds having in excess of millions of species.

State of the Art and Level of Skill in the Art. Although the level of skill in the art is very high, inhibiting enzymes is a very unpredictable art. Kubinyi (3D QSAR in Drug Design: Ligand-Protein Interactions and Molecular Similarity, Vol 2-3, Springer, 1998, 800 pages) teaches that very slight perturbations in the structure of an inhibitor (such as the addition of a methyl group or inversion of a chiral center, see p. 243) can have radical effects on the binding of an inhibitor. Similarly, inhibiting an unknown pathway or biological mechanism is even more unpredictable.

Number of Working Examples and Guidance Provided by Applicant. The applicant provides a data for what appears to be only 4 compounds.

Unpredictability of the Art and Amount of Experimentation. The art of using pharmaceuticals to inhibit enzymes is highly unpredictable as described by Kubinyi. In nearly every case, the skilled artisan could not predict *a priori* whether a given pharmaceutical would inhibit an enzyme. When small variations in structure such as the addition of a methyl group has radical effects on the binding of an inhibitor, without specific guidance or correlations indicating how the structure of species affects its ability to inhibit an enzyme the scope of enablement is constrained to compounds showing substantial similarity to those actually demonstrated to be useful. Furthermore, there would be a huge amount of undue experimentation required in order to synthesize and screen the millions of compounds within the claimed scope. Similarly, if one of ordinary skill in the art does not know what the mechanism of action is, then the unpredictability and amount of experimentation weighs even more towards a non-enabling disclosure for untested compounds.

Considering the above factors, the claims are not enabled for the full scope of the compounds claimed. The examiner recommends either amending the claim scope to only those compounds closely resembling the compounds actually tested and disclosed in the specification or provide additional data and/or structural correlations to guide one of ordinary skill in the art to compounds possessing the asserted utility.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

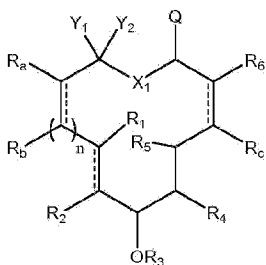
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-5, 7-13, 23-24, 34-35, 49-55, 71-73, and 76-78 are provisionally

rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-42, 45-47 of copending Application No. 10/555152.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they claim subject matter that substantially overlaps in scope. The '152 application claims the genus of compounds of the following formula:



, which is nearly identical to the instant claim scope, but for a few differences in the alternatives in the variable definitions. One of ordinary skill in the art would find these differences obvious because of the substantial structural similarities between the two applications.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

The claims are not in condition for allowance.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is (571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/
Examiner, Art Unit 1626